

EXHIBIT 1

Read this instruction sheet thoroughly before use.

Code No. 439-53901

Wako

HA Series

Creatinine-HA

(Modified Jaffe method)

この商品海外向けの添付文書です。

HA Series Creatinine-HA は本品の輸出用名称です。

This page of the package insert is for use in countries outside of Japan.
HA Series Creatinine-HA is the export name of this product.

Intended use

HA Series Creatinine-HA is an in vitro assay for the quantitative determination of creatinine in serum or urine.

Summary and explanation of the test

Creatinine is produced directly from creatine phosphate or by the dehydration of creatine in the muscles and nerves. The amount of metabolically produced creatinine in the urine is conveniently used to test glomerular function. Therefore, creatinine measurement is one of the essential clinical tests in the diagnosis of uremia and renal diseases, such as renal insufficiency and nephritis, and in monitoring renal diseases.

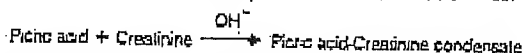
There are various colorimetric methods based on Jaffe reaction. This reagent provides a direct assay with Jaffe method that gives reliable results without the interference from bilirubin.

Reagents

- (1) Alkaline
0.10 mol/L sodium tetraborate
containing sodium hydroxide
Store at below 25°C
- (2) Additional A
0.20 mol/L picric acid
Store at below 25°C
- (3) Picric Acid
6.7 mmol/L 2,4,6-trinitrophenol (picric acid)
Store at below 25°C
- (4) Additional B
containing diethanolamine
Store at below 25°C

Principle of the method

When a sample is added to the reagents, creatinine in the sample reacts with picric acid to yield a reddish-orange color condensate in alkaline solution (Jaffe reaction). By measuring the absorbance change of the reddish-orange color condensate, creatinine in the sample is determined.



Reagent preparation and test procedure

1. Preparation of reagents

R1: Prepare Reagent 1 by mixing one each bottle of Additional A and Alkaline.

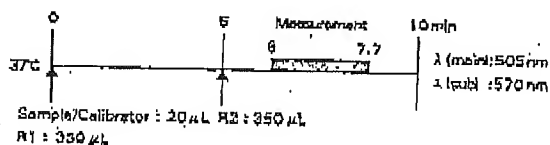
After preparing the Reagent 1, store at 2-25°C and use within two weeks.

See "Precautions on assays".

R2: Prepare Reagent 2 by mixing one each bottle of Additional B and Picric Acid.

After preparing the Reagent 2, store at 2-25°C and use within two months.

2. Standard Procedure



Calibrator: Creatinine Standard Solution (Available separately)
The assigned value of Creatinine Calibrator is traceable to SRM314a (NIST).

<Calculation of creatinine concentration>

Calculate creatinine concentration from the calibration curve which was created from absorbance change of calibrator.

<Application to the various automatic analyzers>

Input the parameters according to the instruction of instruments to perform the measurement. Instrument applications are available upon request.

Precautions on procedure

(1) Samples

- (a) Assay samples immediately after collection.
- (b) Hemolysis gives slightly positive effect on the assay.
- (c) Ascorbic acid and bilirubin do not have significant effects on the assay.

(2) Interfering substances

- (a) Heparin, citrate, oxalate and EDTA do not have a significant influence on the assay when they are used in their usual amounts.

Expected values

Serum	male	0.8-1.3 mg/dL
	female	0.5-0.9 mg/dL

Performance

(1) Sensitivity

- (a) When purified water is assayed, the absorbance change is not more than 0.010 (ΔE/min).

- (b) When a standard of given concentration (creatinine 10 mg/dL) is assayed, the absorbance change is 0.008-0.050 (ΔE/min).

(2) Specificity

- When a control serum or urine of known concentration is assayed, the assay value falls within the range of $\pm 5\%$ of the known concentration.

(3) Precision

- When a sample is assayed not less than 5 times in a run, CV is not more than 5.0%.

(4) Measurable range

- Up to 25 mg/dL creatinine. (In the case of using the standard procedure)

Correlation

Specimen	Serum	Urine
Correlation coefficient	$r = 0.999$ ($n = 50$)	$r = 0.999$ ($n = 55$)
Regression equation	$y = 1.029x - 0.42$	$y = 0.947x + 3.38$
y	HA Series Creatinine-HA (mg/dL)	HA Series Creatinine-HA (mg/dL)
x	Creatinine-Test wako (Jaffe method, mg/dL)	A product of Company A (Enzymatic method, mg/dL)

Precautions on assays

- (1) Do not use the reagents described above in any procedures other than those described herein. Performance cannot be guaranteed if the reagents are used in other procedures or for other purposes.
- (2) Operate the instruments according to operator's manuals under appropriate conditions. Consult the instrument manufacturer for details.
- (3) Store the reagents under the specified conditions. Do not use reagents past the expiration date stated on each reagent container label.
- (4) After opening the reagents, it is recommended to use them immediately. When the opened reagents are stored, cap the bottles and keep them under the specified conditions.
- (5) Do not use the containers and other materials in the package for any purposes other than those described herein.
- (6) If the container of the Reagent 1 is left open for extended periods, the reagent may absorb carbon dioxide in the air causing a decrease in pH and it may give errors on assay. Therefore, the Reagent 1 should be stored in tightly closed container.
- (7) Use Creatinine Standard Solution for calibration. Refer to the instruction sheet in the Calibrator.

Precautions for protection from hazards

- (1) If the reagents come in contact with mouth, eye or skin, wash off immediately with a large amount of water.
Consult a physician if necessary.
The Additional A and the Picric Acid are acidic of which pH is not more than 3.
The Additional B and the Alkaline are alkaline of which pH is not less than 11.

Precautions on disposal

- (1) When discarding the reagents, dispose of them according to local or national regulations.
The Alkaline contains 20.2 g/L sodium tetraborate (4.34 g/L as boron).
The Picric Acid contains 2 g/L picric acid of the phenol.
(2) All the devices including reagents and reagent bottles connected with specimen should be considered potentially infectious.

Precautions on results and diagnosis

This assay should not be used as the sole determinant for clinical diagnosis.

References

- (1) Fabiny, D. L. and Eningshausen, G.: Clin. Chem., 17, 696-700 (1971).
(2) Kouki Tsutsui, Moto Moriwake and Sachie Okayama, Rinsyo Byouin, 10, No. 12, 324 (1971) (in Japanese).
(3) Kouki Tsutsui, Nihon Rinsyo, Fall extra edition, 43, 254-257 (1985). (in Japanese)

Ordering information

Code No.	Product	Package
439-53901	HA Series Creatinine-HA 7150	For 800 tests
	Alkaline	3 × 56 mL
	Additional A	3 × 2.35 mL (3 × for 56 mL)
	Picric Acid	2 × 56 mL
	Additional B	2 × 2.13 mL (2 × for 56 mL)
412-33301	Creatinine Standard Solution (Creatinine: 10 mg/dL)	4 × 5 mL

REV.#1/0401 DDD00K

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